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HLA-typing in Schistosoma Japonicum infection

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George Watt and Nunilon Sy

REPORT NO.

TR - 1049

AD-A201 990

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NOV 03 1988
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UNITED STATES NAVAL
MEDICAL RESEARCH UNIT NO. TWO

APO SAN FRANCISCO, CALIFORNIA 96328

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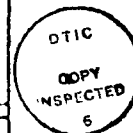
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Scientific Director

This study was supported through funds provided by the Naval Medical Research and Development Command, Navy Department, for Work Unit 3M162770A870 AH315.

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tion medium was used throughout, the discrepancies which occurred between the various plates can only be due to one, or more, of three factors: (a) deterioration in the standard stock solutions of chloroquine phosphate used for dosing the plates; (b) errors in the preparation of the serial dilutions of chloroquine phosphate used in dosing the plates; or (c) deterioration of the chloroquine phosphate after dosing the plate.

Concerning the first possibility, the stock solutions are specially prepared and quality-controlled in a pharmaceutical industry laboratory of impeccable reputation. In longitudinal studies the stock solutions have been shown to be absolutely stable over three years of shelf-life.

Concerning the second possibility, serial dilutions are always made by 2 persons using a standard written protocol, the second person monitoring the actions of the first. Thus the possibility of error is extremely small. Such error would be evident throughout the particular batch and detected through external quality control.

Finally, since the quantity of the drug deposited in the test plate well is extremely small (the highest concentration of the plates under discussion is only 32 pmol/well), deterioration can be expected over time and is known to be enhanced by high ambient temperatures.

Control plates stored at ambient temperature in closed cupboards at WHO headquarters in Geneva have uniformly demonstrated a minimum shelf-life of two years. Similarly, control test plates stored under normal refrigeration in the tropics (Thailand) have shown a similar shelf-life without deterioration. Studies to date indicate that changes do occur at about 3 years even under ideal storage conditions.

From the evidence made available by S. Sinha and A. Gajanana we can only conclude, therefore, that the deterioration they note was probably due to inappropriate storage of the plates and we would like to take this opportunity to impress upon our collaborators who use these plates the importance of proper storage and handling, a point which is stressed in the instructions accompanying the microtest kit.

On a point of technique, we noticed that S. Sinha and A. Gajanana used the MIC as the crucial criterion. Log dose/response regression data were unfortunately not available. Very low schizont counts, as are common at drug concentrations near the threshold level, increase the probability of missing schizonts. The MIC is therefore subject to considerable statistical error and is probably not the ideal quantity for measuring interplate or intraplate variation. Given adequate sample size, an effective concentration (EC) value between EC₁₆ and EC₈₄, e.g. EC₅₀, would probably better reflect such variation.

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6 August 1987

HLA-typing in *Schistosoma japonicum* infection

We were very interested to read about HLA typing in patients with differing clinical manifestations of *Schistosoma japonicum* infection in Leyte, Philippines (Ohta *et al.*, 1987: *Transactions*, 81, 292). We have also wondered why patients seem to have either cerebral or hepatic involvement, but not both, and recently performed HLA typing on 41 schistosomiasis patients and 25 uninfected Filipino controls in an attempt to explore a possible genetic explanation for this phenomenon. Unlike Ohta *et al.*, we observed HLA-B16 in hepatosplenic patients (Table). HLA-B40 was found in both groups. Neither these nor any other HLA-types, either singly or in combination, were significantly more frequent in patients with cerebral schistosomiasis than in patients with hepatosplenic disease or uninfected controls. However, the number of cerebral patients was small because only proven cases were studied.

Table—Prevalence of 2 HLA-antigens in patients with cerebral and hepatosplenic schistosomiasis

	Cerebral (n = 6)	Hepatosplenic (n = 35)	Controls (n = 25)
HLA-B16	1 (17%)	9 (26%)	6 (24%)
HLA-B40	3 (50%)	16 (46%)	14 (56%)

We agree that it is particularly important to investigate the HLA-D region antigens with regard to disease associations (Tiwari & Terasaki, 1981: In: *The Lymphocyte*, New York: Alan R Liss, Inc., pp. 151-163) and look forward to learning the results of further studies by Ohta *et al.* However, we hope that Filipino patients without schistosomiasis will serve as controls rather than the Japanese controls used for the Leyte study. It is also important that cerebral schistosomiasis be carefully defined. In some endemic areas, virtually everyone is infected so that seizures may be associated with, but not due to, schistosomiasis. 64% of patients with schistosomiasis and acquired seizures in our recent study were found to have central nervous system disease unrelated to *S. japonicum* infection (Watt *et al.*, 1986: *Lancet*, ii, 529). Computerized tomography appears to be the most valuable tool for establishing cerebral schistosomiasis as the cause of seizures.

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25 July 1987

Treatment of the acute (toxaemic) phase of schistosomiasis with oxamniquine

In a recent review of clinical experience with oxamniquine, Foster (1987: *Transactions*, 81, 55) presented some data on the treatment of the acute (toxaemic) phase of schistosomiasis that could confuse readers not familiar with the difficulties of treatment of this serum sickness-like disease.

Foster wrote: "A cure rate of 93% was recorded in 15 patients in the acute (toxaemic) phase of the

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SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
1a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED			1b. RESTRICTIVE MARKINGS		
2a. SECURITY CLASSIFICATION AUTHORITY			3. DISTRIBUTION/AVAILABILITY OF REPORT Distribution of this document is unlimited		
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE			5. MONITORING ORGANIZATION REPORT NUMBER(S)		
4. PERFORMING ORGANIZATION REPORT NUMBER(S) NAMRU-2-TR-1049					
6a. NAME OF PERFORMING ORGANIZATION U.S. Naval Medical Research Unit No. 2		6b. OFFICE SYMBOL (if applicable) NAMRU-2	7a. NAME OF MONITORING ORGANIZATION		
6c. ADDRESS (City, State, and ZIP Code) APC San Francisco, California 96528-5000			7b. ADDRESS (City, State, and ZIP Code)		
8a. NAME OF FUNDING/SPONSORING ORGANIZATION Naval Medical Research & Development Command		8b. OFFICE SYMBOL (if applicable) NMRDC	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER		
8c. ADDRESS (City, State, and ZIP Code) Bethesda, Maryland 20814			10. SOURCE OF FUNDING NUMBERS		
			PROGRAM ELEMENT NO. 62770A	PROJECT NO. 3M162770A870	TASK NO. AH
					WORK UNIT ACCESSION NO. 315
11. TITLE (Include Security Classification) (U) HLA-typing in Schistosoma japonicum infection					
12. PERSONAL AUTHOR(S) George Watt, Nunilon Sy					
13a. TYPE OF REPORT Technical Report		13b. TIME COVERED FROM 1987 TO 1988		14. DATE OF REPORT (Year, Month, Day) 1988	
15. PAGE COUNT 1					
16. SUPPLEMENTARY NOTATION Published in the Transactions of the Royal Society of Tropical Medicine and Hygiene, 82:350, 1988.					
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB-GROUP			
			→ HLA-typing; Computerized tomography; Reprints; Schistosoma japonicum; (HT) ←		
19. ABSTRACT (Continue on reverse if necessary and identify by block number)					
→ HLA-typing was recently performed on 41 schistosomiasis patients and 25 uninfected Filipino controls to investigate why patients have either cerebral or hepatic involvement. Neither the following tests HLA-B16, HLA-B40, nor other HLA-typing were significantly frequent in patients with cerebral schistosomiasis. Keywords: Biology; diagnosis medicine.					
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION Unclassified		
22a. NAME OF RESPONSIBLE INDIVIDUAL RAM I. Groves, M.			22b. TELEPHONE (Include Area Code) 301/663-7567		22c. OFFICE SYMBOL NMRDC

DD Form 1473, JUN 86

Previous editions are obsolete.

S/N 0102-LF-014-6603

SECURITY CLASSIFICATION OF THIS PAGE

Unclassified